

Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

Remarks

Claims 1-21 and 23-42 are pending in the present Application. In response to a previous Restriction Requirement filed June 13, 2008, Applicant elected with traverse claims of Group II, including claims 13-24 and elected with traverse in species elections compound ML464, and melanoma as a specific cancer cell type. Applicant also indicated that claims 13-21 and 23 encompassed the elected species. In the present Office Action, the PTO considers Claims 1-12, 15-17 and 25-42 as withdrawn as being drawn to a non-elected invention. Furthermore, the PTO states that Claims 13-14, 18-21 and 23-24 are presently under consideration.

Information Disclosure Statement

Applicant acknowledges the PTO's receipt of the Information Disclosure Statement (IDS) filed August 3, 2007, and requests that the PTO point out any alleged deficiency in the IDS.

In the Office action, the PTO states that "the Examiner has considered the reference cited therein to the extent that each is a proper citation" and has also stated on the IDS form 1449 appended to the Office action that "all references considered except where lined through." However, the undersigned attorney was unable to identify any reference that was lined through by the PTO on the appended IDS form 1449. Accordingly, Applicant respectfully requests that the PTO specify the reference(s) it deems to be not a "proper citation" and invites the Examiner to contact the undersigned attorney in this connection.

Election/Restrictions

Applicant acknowledges the PTO's decision to make final the Restriction Requirement. However, Applicant requests rejoinder of Claims 15-16 with the present set of claims receiving examination on the merits, for reasons provided below.

Claim Interpretation

Applicant requests rejoinder and examination of Claims 15-16 with the present set of claims because of incorrect claim interpretation by the PTO.

In the Restriction Requirement of May 13, 2008, the PTO required, *inter alia*, election of “a single cancer cell type or single specific tumor species as appropriate e.g. melanoma cells or melanoma...” Applicant, in response, elected melanoma. In the present Office Action, the PTO states that “Examiner is interpreting the tumor cell being inhibited as the elected melanoma tumor cells and the organ comprising the cells to be the tissue of origin. Since the tissue of origin for the applicant’s elected tumor cell specie ‘melanoma’ is the skin, claims 15 and 17 which recite the skeletal system of the subject as the organ system are withdrawn from consideration.” Applicant respectfully disagrees with the PTO’s interpretation. The PTO appears to interpret these claims as directed to melanomas originating in skeletal or bone tissue. However, it is Applicant’s position that Claims 15-16 encompass tumor cells that originate in non-skeletal tissues such as skin but invade skeletal or bone tissue. Applicant, accordingly, requests reconsideration and withdrawal of the PTO’s claim interpretation, and further requests rejoinder and examination of Claims 15-16 with the claims receiving examination.

Claim rejections under 35 USC § 112 first paragraph for enablement

In the present Office Action, the PTO rejects Claims 13-21, and 23-24 as allegedly not enabled because of recitation of “preventing” in claim preambles. The PTO further states that “Amending the claims to recite ‘A method for inhibiting melanoma tumor cell growth...’” (i.e., deleting “preventing”) would overcome the rejection. In order to advance prosecution, Applicant herein amends the claims to address the Examiner’s concerns, without conceding the merits of the PTO’s reasoning. Applicant, accordingly, requests reconsideration and withdrawal of the rejections under 35 USC § 112 first paragraph for enablement.

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Claim rejections under 35 USC § 112 second paragraph

In the Office Action, the PTO rejects Claim 14 as allegedly indefinite for recitation of the term “tumor cell is comprised by.” It is Applicant’s position that this phrase is not indefinite. However, in order to advance prosecution, Applicant amends Claims 14-16 with alternative phrasing, with no intent to alter the scope of these Claims. Applicant therefore requests reconsideration and withdrawal of the rejection.

Claim rejections under 35 USC § 103

In the Office Action, the PTO notes that there are joint inventors, and the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made. In response, Applicant asserts that that all claims were commonly owned at the time the invention was made.

In the Office Action, the PTO rejects Claims 13-14, 18-21 and 23-24 as allegedly obvious under 35 USC § 103(a), in view of the combined teachings of Fisher et al. (US Patent 6,291,469, “Fisher”), Pitts et al. (US Patent 6,489,333, “Pitts”) and Trikha et al. (Cancer Research 57: 2522-2528, 1997 “Trikha”). Applicant requests reconsideration and withdrawal of the rejection, because the PTO has not established a *prima facie* case of obviousness for any claim.

In order to establish a *prima facie* case of obviousness of a claim, the PTO must show that a) a cited reference, or combination of references, teaches or suggests each and every claim element; b) there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; and c) there is a reasonable expectation of success. MPEP § 2142.

In the present case, the PTO does not establish that cited references provide a reasonable expectation of success. In the Office Action, the PTO describes Fisher as teaching spiro compounds that block GPIIb/IIIa fibrinogen receptor (same as $\alpha IIb\beta 3$ receptors), and thereby inhibit platelet aggregation and subsequent thrombus formation. The PTO describes Pitts as teaching heterocycles that are useful as antagonists of the $\alpha v\beta 3$ and $\alpha IIb\beta 3$ integrins and methods

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of using the compounds for the inhibition of cell adhesion, treatment of antigenic disorders, inflammation, bone degradation, cancer metastasis, and other conditions mediated by cell adhesion and/or cell migration, and furthermore teaches that tumor dissemination, or metastasis, involves penetration and transversion of tumor cells through basement membranes and the establishment of self-sustaining tumor foci in diverse organ systems. The PTO further characterizes Pitts as teaching that development and proliferation of new blood vessels are critical to tumor survival, and that inhibition of angiogenesis in animal models has been shown to result in tumor growth suppression and prevention of metastatic growth. The PTO further characterizes Pitts as setting forth the concepts that an inhibitor which acts against all agonists would represent a more efficacious antiplatelet agent than currently available anti-platelet drugs which are agonist specific, and that platelet glycoprotein IIb/IIIa provides a common pathway for all known agonists, and furthermore teaches compounds that bind to integrin receptors and thereby alter cell-matrix and cell-cell adhesion processes and are useful for inhibition of cell adhesion and treatment of cancer metastases among other indications. The PTO describes Trikha as teaching that melanoma cells possess an intracellularly localized pool of high-affinity α IIb β 3 receptors, and that B16a melanoma cells express the α IIb β 3 integrin.

The PTO asserts that it would have been *prima facie* obvious to combine Fisher's teachings of spiro compounds which are platelet-specific activated α IIb β 3 receptor antagonists, Pitt's teachings of use of integrin antagonists for inhibition of cell adhesion and treatment of cancer metastases, and Trikha's teachings of expression of α IIb β 3 receptors in melanoma cells to reach the presently claimed methods, that the solutions to the prior art problems provide a motivation to combine the references, and that a skilled artisan would be imbued with a reasonable expectation of success.

The references cited by the PTO do not provide a reasonable expectation of success. As set forth in the specification, for example on page 36, lines 10-13, the present claimed methods derive at least in part from the inventors' discovery that inhibition of metastasis into bone through inhibition of α IIb β 3 receptors can result from the microenvironment: "The inhibition of the bone metastasis seen in the β 3 $^{-/-}$ mice reflect a bone *microenvironment* unable to support tumor cell growth." (emphasis added). In contrast, the PTO points to no text in any of Fisher, Pitts, or Trikha that teaches or suggests that the bone microenvironment affects the susceptibility

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of bone tissue to development of metastatic tumors, which is required to establish a reasonable expectation of success. Although the PTO cites Fisher for teaching spiro compounds and a method of preventing or treating thrombosis and other indications wherein “platelet aggregation inhibitors of the invention have potential uses,” platelet aggregation is a phenomenon that occurs apart from the bone microenvironment. Furthermore, although the PTO cites Pitts as teaching that inhibition of angiogenesis in animal models of cancer has been shown to result in tumor growth suppression and prevention of metastatic growth, angiogenesis is a phenomenon that occurs apart from the bone microenvironment. In addition, although the PTO cites Trikha for teaching that melanoma cells possess α IIb β 3 receptors, the presence of α IIb β 3 receptors *vel non* in melanoma cells is irrelevant to the practice of the present claims.

The PTO thus has not shown that the cited references, either individually or in combination, provide a reasonable expectation of success, and therefore has not established a *prima facie* case of obviousness. Applicant, accordingly, requests reconsideration and withdrawal of all claim rejections under 35 USC § 103.

Conclusion

As it is believed the application is in a condition for allowance, Applicant requests prompt and favorable action. All amendments, withdrawals and cancellations are made without prejudice or waiver.

If the PTO deems the claims not to be in condition for allowance, the Applicant requests the Examiner contact the undersigned attorney to schedule an interview before mailing an Office Action. Any communication initiated by this paragraph should be deemed an “Applicant-Initiated Interview.”

Because this response is submitted within the shorten statutory period for reply set to expire three months from the mailing date of October 3, 2008, Applicant believes that there is no fee due. However, if the PTO determines that a payment is due, the Commissioner is hereby authorized to credit any overpayment or to charge any deficiency in connection with this application to Deposit Account 19-3140.

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Respectfully submitted,

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